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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/796,292	03/10/2004	Kunwar Shailubhai	122069-40308707	9377

909 7590 03/20/2008

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EXAMINER	
GEMBEH, SHIRLEY V	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
03/20/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/796,292	SHAILUBHAI ET AL.	
	Examiner	Art Unit	
	SHIRLEY V. GEMBEH	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,12,21,22,25-30,33,35-37 and 39-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,12,21,22,25-30,33,35-37 and 39-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed **12/14/07** presents remarks and arguments to the office action mailed **6/14/07**. Applicant's request for reconsideration of the rejection of claims in the last office action has been considered.

Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Applicant's request to show specie election that were searched. The searched was broadly performed inclusive of wide variation of cancer, the individual cancers such as breast, prostate, leukemia, malignant carcinoma, colon and ovarian was done.

Information Disclosure Statement

Applicant argues that items C1 and C6 of the IDS corresponds to International Search Report for PCT/US04/07144 and supplementary European search report EP 04 71 9198.

Items C1and C6 remains unconsidered because they are not considered published documents. Individual prior art identified in the search note should be listed and not refer to the search record.

Status of claims

Claims 11-12, 21-22, 25-30, 33, 35-37 and 39-48 are pending in this office action.

Allowable Subject Matter of claims 33 and 39-45 is withdrawn because of the double patenting rejection.

Maintained Claim Rejections - 35 USC § 103

Applicant argues that Rice does not teach the claimed compound, that the Rice reference compounds have either two ethyl or two methyl substituent and that the compounds do not contain 5 or more carbon atoms and there is no teaching or suggestions to modify the compound to produce the claimed compound.

In response this is found unpersuasive because the Rice reference teaches that introductory of a methyl group at these positions increase the inhibitory effect five folds in human mammary cancer and suggested further substitutions. See page 731, left. col. under abstract, lines 4-8. Based on such a teaching one of ordinary skill in the art would have been motivated to explore other alkanes at that position. Also, rice does not have to teach the exact compound. Motivation comes from other teachings to modify the compound.

With regard to the statement that Mirabelli does not teach the compound. In response, the compound of Mirabelli was used to show that these azaspine compounds are known to inhibit cancer. Comparing metal-containing compound with a

non metal containing compound has no bearings to the claim invention. The reference used cancer cell to show the inhibitory effect. Cell lines such as colon cells were used. Colon cancer is a solid cancer. In the introductory the teachings are inclusive of leukemia, prostatic and mammary carcinomas (breast cancer). See page 231, rt col. lines 3 -4 and also abstract. The reference further teaches that increased cytotoxic potency within the group of Carbon containing analogs was directly related, to increase in the length of 'the alky1 group(s). See abstract lines 7+. Thus motivation to one of ordinary skill in the art to modify the compound to have more alkyl groups which is inclusive of the claimed invention for decrease cytotoxicity as taught by Mirabelli, see abstract, line 7-8. As to the claimed cancers the reference refers to prostate and mammary cancer in the teaching.

With regards to Badger, Applicant traverses that the art do not teach treating cancer and the teaching of Nakashatri showing cytokine IL-1α does not remedy the deficiencies.

This is found unpersuasive, the compound is taught by Badger and it is known that increasing the alkyl substituents makes the compound less toxic, one ordinary skill in the art would have been motivated to combine the known knowledge in the art, modify the compound of Rice and Mirabelli to the compound of Badger and used in the treatment of cancers breast cancer for example because Nakashatri et al, showed that cytokine Il is responsible in majority of node positive breast cancer. Since Badger teaches the compound is a cytokine inhibitor. One of ordinary skill in the art would have been motivated to use the teaching of Nakshatri because it is well known in the art

that breast cancer is an inflammatory cancer and cytokines are responsible for inflammatory disease absent factual evidence.

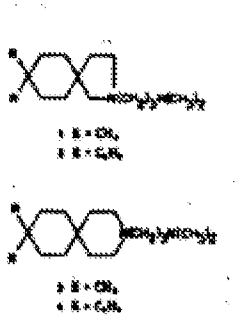
The Dagger reference was used to show the maleate salt of the drug.

Careful consideration has been given, however, found not persuasive. The rejection is maintained as in the last office action of record and repeated below to incorporate newly added claims.

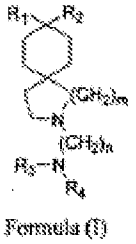
Claims 11-12, 21-22, 25-30, 35-37 and newly added claims 46-48 are and remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rice et al. J. Heterocyclic Chem., 10(5):731-735 (1973) (applicants prior art submission) taken with Mirabelli et al. Anti-Cancer Drug Design, 3(4):231-242 (1989) (also Applicant prior art submission) in view of Badger et al. US 5,602,166 and Dagger et al. US 5,939,450.

** Consideration of the abstract of Rice et al. has failed to reveal citation of the N,N-dimethyl... drug as explained below. Therefore citing this in Rice et al. appears improper. If the abstract pf Rice et al. cites a compound name that is different from that of instant claim 11, this needs to be explained to support this rejection.

Rice et al. teach the drug N,N-dimethyl-8,8-dipropyl-2-azaspirol[4,5]decane a member of the class of drugs azaspirane (see abstract) for the treatment of cancer where in the drug showed a significant inhibition of cancer cell growth in human mammary cancer cells (inclusive breast cancer). The compounds of Rice has N,N



as that of the claimed compound even though named differently

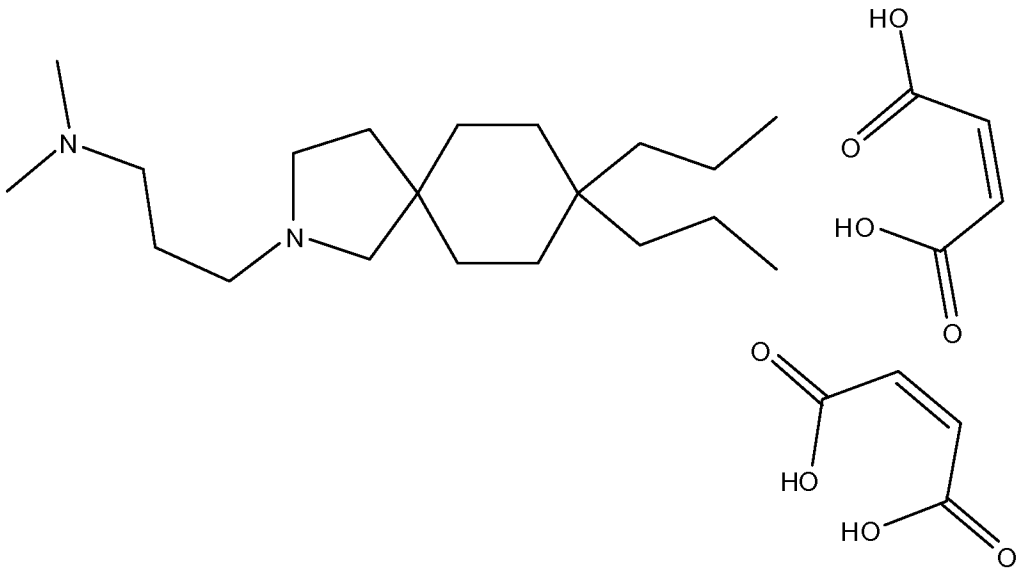


Formula (I)

but are the same. Thus the teaching is inclussive of R (1-4).

Mirabelli et al. teach structurally related azaspiranes in the treatment of cancer, wherein N,N-dimethylaminopropyl-2-aza-8,8-diethyl-8-germaspiro[4,5]decane is used together with other chemical drugs that are obvious variation of the claimed drug in the instant claim 11 was used to determine in vitro and in vivo activity (see page 234) as in the instant claim 11-12, wherein the cancer is a mammary adenocarcinoma (Mammary adenocarcinoma are cancers that begins in cells that line the inside of organs. They begin in cells that make milk) as evident by breastcancer.org (2001). The reference Mirabelli et al. teach breast cancer, and prostate cancer (see page 231) as in claim 12, wherein the cancer is breast, prostate (see page 231) and colon cancer (see page 232) as in claim 35. With regards to claims 12, 21-22 and 37 regarding the structure, Applicant should note that a specie election has been made and the compound elected is the result of the varying substituents of R. Thus obvious of teaching of claims 46-48.

Badger et al. teach N,N-dimethyl-8-8-dipropyl-2-azaspiro[4,5]decane-2-propanamine is a cytokine inhibitor (as required by instant claims 11-12, 21-22, 25-26 and 46-48, see col.s 1 and 2.. Cytokines have been found to play a major role in the control of estrogen in breast cancer. As evident by Nakshatri et al, showed cytokines induce nuclear factor-κB (NF-κB) identified IL-1 as the factor responsible for NF-κB activation of fibroblast. Analysis of the primary breast carcinomas showed the presence of IL-1 transcriptase in the majority of lymph node-positive breast cancer. Therefore the teaching of Badger would have resulted in using the compound N,N-dimethyl-8,8-dipropyl-2-azaspirol[4,5]decane-2-propanamine salt for the treatment of breast cancer in humans (see abstract and see col. 6, lines 54-55) as in claim 26, but fail to teach the dimaleate salt, wherein the drug is administered orally or parenterally (see col. 6, lines22-23) as in claims 27-28) in the amount of 0.1 mg-100/kg mg per day (see col. 6, lines 29-35) to a human (see col. 6, line 6) as in claims 29-30). The compound elected



is 3-(8,8-dipropyl-2-azaspiro[4.5]decan-2-yl)-*N*,*N*-dimethylpropan-1-amine dimaleate

.

and would have resulted from the compound of formula I (see col. 2, lines 3-30). Note that R (1-2) are straight chain alkyl, R(3-4) are the same containing one carbon atom- a methyl group. (The maleate form of the compound was taught by US 5,939,450 by Dagger et al. see col. 1, lines 8-25) where the exact compound is taught.
Although, the Rice et al. reference, fail to use the exact compound of the above structure, one of ordinary skill in the art would have been motivated to make and use the dimaleate form of the class of compounds as taught by Dagger et al. and use for the treatment of cancer in general as taught by Rice. Even though, no specific cancer type was taught, the generic teaching would suggest to one of ordinary skill in the art to make and use for the treatment to treat breast, colon and prostate cancer because Mirabelli et al. used compounds of azaspirane to treat these types of cancer. The drug of above structure falls in the class of azaspirane. Therefore one of ordinary skill in the art would be motivated to switch the compound of Rice et al. or Mirabelli et al. to the compound of Dagger et al. treat colon, breast and prostate cancer and expect a successful result in doing so because the art has used close structural similarity (homologs) of the reference compound for the treatment of these cancers.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

** Please insert the claims of 10548794 on which the ODP is based in the below rejection statement.

The Claims of 10548794 on which the ODP is based in the below rejection statement.

Claims 11-12, 21-22, 25-30, 35-37 and 46-48 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent Application No. **10548794**. Although the conflicting claims are not identical, they are not patentably distinct from each other. The reasons are as follows:

- Both sets of claims refer to treating cancer such as leukemia melanoma, breast cancers in the current application (claims 11-12, 21-22, 33, 25-30, 35-37 and 46-48) and tumors (claims 1 – 20) in the copending application. The current application claims are obvious variation of copending application claims
- • Both applications recite using the same compositions and/or derivatives thereof. See current application claims 11-12, 21-22, 33, 25-30, 35-37 and 46-48 and copending application claims 1 – 20. The compositions recited in the claims are obvious of each other.
- As to the copending application claims 14-16, these claims refer to a the

functions of the compound, one cannot strip the characteristic of a compound. As

recited in the MPEP ." A chemical composition and its properties are inseparable.

Therefore, if the prior art teaches the identical chemical structure, the properties

applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). With regard to a kit The printed matter on a label or package insert of a kit or container does not lend patentable weight as a limitation of the claimed product, composition, or article of manufacture, absent a functional relationship between the label or package insert of a kit and the product, composition, or article of manufacture of a kit or container.

In view of the foregoing, the copending application claims and the current application claims are obvious variations.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHIRLEY V. GEMBEH whose telephone number is (571)272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SVG
2/25/08

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614